Reconsideration is respectfully requested of the rejection of claims 1, 2, 4-10, 12-50, 72-75, 84, and 86-90 under §103(a) as unpatentable over the AAPS reference in view of Black.

Claim 1 is directed to a pharmaceutical composition comprising one or more discrete solid orally deliverable dose units, each comprising particulate celecoxib in an amount of about 10 mg to about 1000 mg in intimate mixture with one or more pharmaceutically acceptable excipients, and having a distribution of celecoxib particle sizes such that D_{90} of the particles is less than 200 μm; said composition exhibiting upon oral administration a relative bioavailability not less than about 50% by comparison with an orally delivered solution containing celecoxib at the same dosage rate.

The AAPS reference is a short abstract of a scientific paper relating to the disposition kinetics and biotransformation of celecoxib (referred to in the abstract as "SC-58635") in man. The AAPS reference states the following:

> "**Subjects received** a single oral 300 mg dose of [^{14}C]-SC-58635 (100 μCi) as a fine suspension followed by **300 mg of SC-58635 as a capsule** after a 15-day washout period. ... Total [^{14}C] and unchanged **SC-58635 were readily absorbed with c_{max} values of** 1527 (638) and **1077 (649) ng/mL**, respectively. **The T_{max}, $t_{1/2}$ and $AUC_{(0-48)}$ values for SC-58635 were 1.9 (0.6) hours, 15.6 (3.5) hours and 8763 (2274) ng/mL * hours.**" *(emphasis added)*

The Office states, on page 3 of the May 17, 2005 Office action, that "AAPS teaches a celecoxib (COX-2 inhibitor) formulation that exhibits a c_{max} values of 1527 and 1077 ng/mL, and a T_{max} of 1.9 hours." Applicants respectfully draw the Office's attention to the data shown above, and points out that the c_{max} value of 1077 ng/mL refers to unchanged celecoxib, while the c_{max} value of 1527 ng/mL refers to total [^{14}C] – that is, it is not limited to unchanged celecoxib.

Nowhere does the AAPS reference describe or suggest whether the capsule containing celecoxib comprised excipients. Nor is any mention or suggestion made of whether the celecoxib is particulate, much less whether the celecoxib has a particle size distribution as set forth in claim 1, above.

As noted by Applicants in the IDS filed on February 24, 2005, the AAPS reference (referred to in the IDS as "the Karim et al. reference") was previously submitted to the Office in the IDS dated April 26, 2002; that Applicants were resubmitting the reference in the February 24, 2005 IDS to particularly draw the Examiner's attention to it; and that Applicants noted that the data reported in the reference are substantially similar to the data reported in Example 13 of the instant specification.

Black discloses that 2-(3,5-difluorophenyl)-3-(4-(methyl-sulfonyl)phenyl)-2-cyclopenten-1-one is useful as a COX-2 inhibitor. Black further discloses that this compound may be administered orally, topically, parenterally, by inhalation spray or rectally (see page 2, lines 2-4). Various pharmaceutical compositions suitable for several of these routes of administration are described, see, e.g., page 2, line 10 through page 3, line 21. Nowhere does Black describe or suggest celecoxib or compositions comprising celecoxib. Nowhere does Black suggest a composition comprising about 10 mg to about 1000 mg of particulate celecoxib having the particle size distribution as set forth in claim 1, wherein the celecoxib is in intimate mixture with one or more pharmaceutically acceptable excipients, and where the composition has the required relative bioavailability.

A *prima facie* showing of obviousness requires, *inter alia*, that the cited references describe or suggest every limitation of the claimed invention. See MPEP 2143. Applicants respectfully assert that the Office has not made a *prima facie* showing that claim 1 is obvious in view of the AAPS reference and Black. The Office has not because it cannot.

A reference "may qualify as a prior art reference under §103, but **only for what is disclosed in it**." Reading & Bates v. Baker Energy Resources, 748 F.2d 645, 652 (Fed. Cir. 1984) (emphasis added). In Reading & Bates, "the mere fact that [a] one-page promotional brochure boasts the ability and results of a process" was not sufficient to be an enabling disclosure of that process. Id. For similar reasons, Applicants assert that if the AAPS reference is prior art against the claims of the subject application, it qualifies as prior art only for what is disclosed in it. The AAPS reference merely discloses that 300 mg of celecoxib were administered "as a capsule" and the pharmacokinetic parameters c_{max}, T_{max}, $t_{1/2}$ and $AUC_{(0-48)}$ observed upon such administration. The reference is silent as to the nature of the celecoxib, including whether it is in particulate form and if so, what the particle size distribution is. Indeed, as the Office noted, "AAPS does not expressly teach the particle size distribution... ."

Applicants respectfully submit that the combination of what is disclosed in the AAPS reference and Black do not recite every element of claim 1, and that therefore the Office has not shown that claim 1 is *prima facie* obvious in view of these references.

The Office asserts that "the burden is shifted to applicant to show that the formulation of AAPS does not have the claimed particle size distribution, as well as the detrimental effect and/or unexpected results over the particle size distribution, because AAPS teaches the oral formulation of celecoxib having the claimed c_{max} and T_{max} values." Applicants respectfully submit

that because the Office has not shown that claims 1, 2, 4-10, 12-50, 72-75, 84, and 86-90 are *prima facie* obvious, shifting the burden to Applicants is improper. See MPEP 2142. Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 4-10, 12-50, 72-75, 84, and 86-90 be withdrawn.

Applicants respectfully acknowledge the Office's comments regarding claim 3. However, in light of the comments above, Applicants respectfully assert that claim 1 is not obvious, and is patentable, and therefore respectfully request that the objection to claim 3 be withdrawn.

Applicants submit that the present invention is now in condition for allowance. Early allowance of all pending claims is respectfully solicited.

Respectfully submitted,

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Enclosures:

FacsimileTransmittal Letter
Combined Amendment Transmittal and
Request for Extension of Time
Reqeust for Continued Examination